THE MANAGEMENT OF CARCINOMA OF THE CERVIX UTERI*

BY BERNARD R. MOONEY

Winnipeg

THE management of carcinoma of the cervix can be conveniently considered under three headings: (1) diagnosis; (2) treatment; (3) follow-up. Observations on the first two are based on a group of 115 patients treated at the Winnipeg General Hospital in the three-year period from November 10, 1937, to November 10, 1940. It is felt that no remarks worth while could be made at this time regarding the follow-up of these cases.

The x-radiation used in all cases was produced by a 400 kv. machine. Daily records were kept of the dosage, and the condition of the patient while undergoing treatment. Progress notes include weekly complete blood counts, cell volume, icterus index, and sedimentation rate, and frequent pelvic examinations.

It is reasonable, I believe, to state that in the Province of Manitoba under the Cancer Relief and Research Institute the facilities for treating cancer are adequate so far as radium is concerned, but x-ray equipment according to a study of present conditions would have to be doubled at least. The registered death rate from cancer is gradually climbing until in 1939 it stood second in the five leading causes of death. Fig. 4 illustrates this point. This gradual increase in the registered death rate from cancer in general applies to cancer of the cervix as well.

DIAGNOSIS

Unfortunately in the great majority of cases the disease is in an advanced stage when the patient is first seen by the doctor, and there is very little difficulty in arriving at a clinical diagnosis. Biopsy is always advised both for histological grading and for accurate diagnosis. Clinical stages and pathological grades are as follows:

Clinical Stage I.—Primary lesion limited to the cervix.

Clinical Stage II.—Primary lesion in cervix with moderate extension into parametrium or vaginal wall. Uterus freely movable.

Clinical Stage III.—Primary lesion extending well into parametrium with fixation of the uterus.

Clinical Stage IV.—Advanced disease with fixation of the uterus or distant metastasis.

The pathologist classifies the neoplasm into Grades I, II, and III according to the histological picture.[2]

Grade I.—Adult type made up of highly differentiated cells with tendency to cornification and formation of pearls. Radio-resistant.

Grade II.—A plexiform type in which the cells have lost most of their squamous character, show a plexiform arrangement, a tendency to infiltration, and a moderate degree of anaplasia. More radiosensitive.

Grade III.—The anaplastic type in which the cells have lost all squamous character are completely undifferentiated and diffusely invasive. Highly radiosensitive.

Fig. 1 shows graphically the percentage of patients grouped in clinical stages I, II, III and IV; and Fig. 2, the microscopic grading into grades 1, 2 and 3.

There seems to be some difference of opinion regarding the response of the different histological grades to radiation.[11] It is true that surgical results may be better in grade 1 and worse in grades 2 and 3, but experience has established that this is not true of radiation treatment. Some authorities produce evidence that grades 1, 2, and 3 give about the same five-year survival rate when radiologically treated.[1] We feel, however, that in the plan of treatment the clinical stage of the disease deserves more attention than the histological grade.[15]

Early diagnosis always needs to be stressed. Whatever may be the etiological factors in carcinoma of the cervix there is no doubt that abnormal vaginal bleeding is by far the most common and earliest warning. The slightest amount of this bleeding, or blood-tinged discharge, should excite suspicion and call for immediate and careful investigation, including biopsy if the cervix presents a doubtful area. Abnormal discharge from the vagina is also worthy of the closest scrutiny.

Just how much delay in diagnosis is due to the patient's ignorance of the early symptoms and how much to lack of financial means to pay for the treatment is difficult to estimate,

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but it is surprising and depressing to hear so often, this statement: "The reason I did not go to the doctor sooner was because I was afraid of the expense of the treatment".[9]

TREATMENT

In planning the treatment of carcinoma of the cervix there are a few important principles to consider. The amount and filtration of the radium used and the dosage and time required for the x-ray series must be planned for each patient. The general physical condition of the patient, including the age, is important. A patient debilitated by hæmorrhage and infection, should be restored by transfusions and medical measures to a condition in which she will stand x-ray and radium treatment; otherwise, the radiation itself may do more harm than good. Elderly women with degenerative disease and the young have a poor prognosis. Fig. 3 illustrates the number in each age group. The plan of procedure will also depend on the following conditions in about the order named: (*a*) the clinical stage of the growth; (*b*) whether or not pyogenic infection is present; (*c*) the histological grade; (*d*) whether or not the lesion is fungating or is of the ulcerating or evacuating type. Unfortunately also, we have to consider the patient's economic status, that is, how long can she afford to live away from home. Repeated inadequate treatments with radiation, x-ray or radium should be avoided if at all possible. The first attack is the important one. Radiation tinkering is quite as dangerous and unsuccessful as surgical tinkering.[12]

We must first endeavour to prevent the spread of the carcinoma by metastasis and local invasion, and every means at our command should be made subservient to that aim. Patients do not die of the local lesion as a rule, but they do die from extension of it, permeation of vital structures, and from distant metastasis. Next to the cancer itself, the unsuccessful treatment of carcinoma of the cervix is due to infection, and the leader in this group is sepsis of the urinary tract.

Our plan of action then, is to restore the patient to a good physical condition if indicated, control pyogenic infection if possible, and attempt to prevent extension of the local disease by metastasis and local permeation. The time required for the total treatment need not be extended, because x-radiation can safely be given at the same time as the above local and general measures are going on.[13] A large fungating infected vaginal mass, in which it is difficult or impossible to locate the cervical canal, can be destroyed by x-radiation and the subsequent insertion of radium converted into a simple procedure.

MANAGEMENT ACCORDING TO THE CLINICAL STAGE

Clinical Stage I.—Primary lesion confined to the cervix. Three methods of treatment are at present indicated: (*a*) radium; (*b*) x-radiation; (*c*) surgery.

Radium only is perhaps the most commonly used, and, theoretically, should be all that is necessary if one is sure that the disease is confined to the cervix. In practice, however, when there is any doubt it is often considered safer to advise a complete course of x-radiation.

X-radiation only, using an intra-vaginal cone placed in contact with the lesion, is now used in some centres where proper equipment and personnel are at hand. I have had no experience with this method but, according to the literature, it is scientifically correct and has some advantages.[8, 10]

Surgical operation. In the three-year period mentioned above the records of the Winnipeg General Hospital show that four cases were treated by operation. In each case the malignant lesion was apparently not the primary reason for the operation, because a Stürmdorf operation was done on two occasions and an amputation on the other two.

Clinical Stage II. — Primary lesion in the cervix with moderate extension to the parametrium or vaginal well; uterus freely movable.

In this stage it is now generally agreed that radium alone cannot be depended on to control the disease and x-radiation is added either before, during, or after the application of radium.[14] Fig. 5 is a summary of the distribution in this series of patients. Many authorities[3, 4, 5, 7] think that the complete x-ray course should be given first in order to destroy or devitalize cancer cells, minimize the local process, and reduce the danger of metastasis. This, in the light of the known local action of radium, seems a sound procedure. Another advantage is that infection, which very commonly complicates the picture, can be cleared up during the x-ray treatment and before radium is inserted. The intense local action of the radium, where the

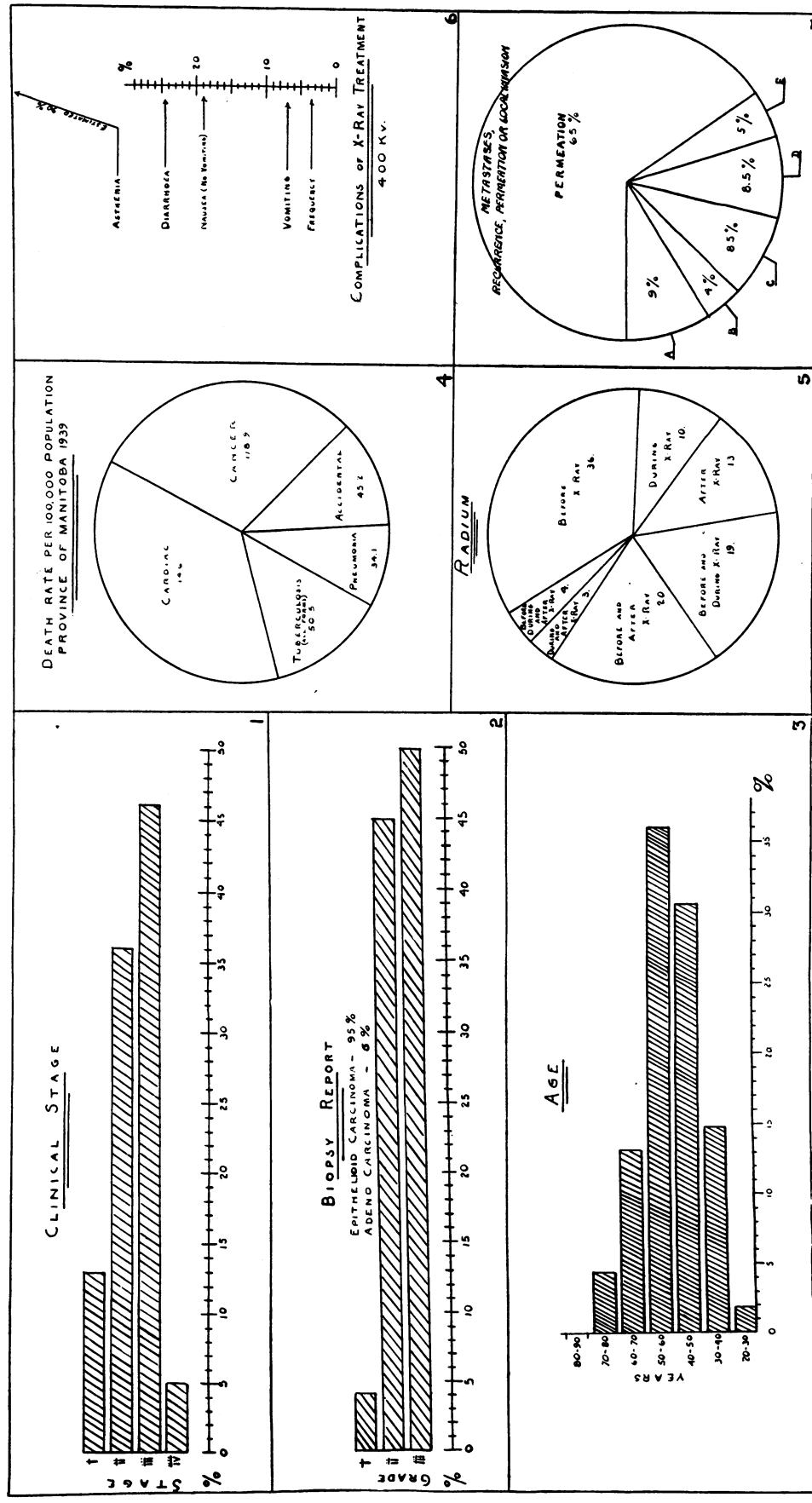

Fig. 5.—Briefly the plan of x-radiation treatment was as follows: 400 kv., 5 ma., 7 mm. copper filter, 55 cm. distance, 6 areas, size of each area 15 x 15 cm., 300 r. a day, 40 to 50 treatment days; total dose—12,000 to 15,000 r. (The radium applicator commonly used is made of two 50 mg. tubes in tandem—sometimes 10 mg. tube in each fornix. The filter is 1 mm. platinum, 1 mm. brass and rubber tubing. The total dosage is between 5,000 and 6,000 milligram hours, given usually in two applications). **Fig. 7.**—(A) Metastases; (B) recurrence and metastases; (C) recurrence; (D) permeation and metastases; (E) permeation and recurrence.

applicator is in direct contact with the cervical canal, of necessity results in a destruction amounting to a slough. A combination of a radiation slough and pyogenic infection is a serious matter and should be avoided if possible.[6] Another argument in favour of x-ray first is that the trauma of dilating the untreated cervix may allow viable cancer cells to enter the general circulation.

Clinical Stage III.—Primary lesion extending well into the parametrium with fixation of the uterus. Generally speaking, the remarks made regarding Stage II apply in this stage and to a greater degree.

Clinical Stage IV.—Advanced disease with fixation of the uterus or distant metastasis. The maximum accomplishment of radiation treatment in patients with advanced disease is, as a rule, only palliation in an effort to make the patient as comfortable as possible under the circumstances. Occasionally a rather surprising temporary response will occur, and a few five-year survivals have been reported.

In the treatment of carcinoma of the cervix uteri x-radiation has not so far taken a very prominent position except in a few centres. Some of the reasons for this are easy to understand. It is only recently that trained radiation therapists in sufficient numbers, and satisfactory x-ray equipment have been available. Radiation physicists, qualified to measure the output of tubes and depth dose, using different voltages and filters, are only now available in many sections of Canada. Now it is more generally realized that a patient receiving a large dose of x-radiation, such as is necessary in cancer of the cervix, has to be carefully watched. The radiologist should be present at these treatments and adjust the dose to the patient, not the patient to the dose.

The complications of the x-ray treatment itself, as I have observed them, are asthenia, diarrhœa, nausea, vomiting, frequency and skin changes. These are summarized in Fig. 6. Some are more marked when using 400 kv., and others are more pronounced with 200 kv. None of them are serious enough to interfere with the treatment. A little tact and attention should be devoted to them however. Nausea, vomiting, and skin reactions are noticeably less, using 400 kv., but diarrhœa, frequency of urination and general weakness are somewhat more troublesome. Blood changes are approximately the same. In about 150 patients we have done weekly blood studies including complete cell counts, cell volume, sedimentation rate, and icterus index. This investigation will be reported later, but, in general, it may be said that there is no change in the red cell count or hæmoglobin estimation that could be considered due to radiation. The neutrophile and lymphocyte count shows an initial drop, a subsequent fluctuation, and returns to normal after treatment. In treating the pelvis with super voltage diarrhœa is the rule; if radium is used during the x-ray series the diarrhœa is increased and may occasionally become troublesome and prolonged. I have seldom found it necessary to interfere with or discontinue treatment on account of diarrhœa. Quite often it clears up while the course is in progress, and I have come to look upon it as a good indication that the dose is being delivered in the depth as it should be. I think it is much safer and less distressing to the patient if x-ray and radium are not given at the same time.[16]

The incidence of metastasis, recurrence, and local invasion from the initial lesion are compared in Fig. 7.

REFERENCES

1. BOWING, H. H.: Carcinoma of the cervix, *Minnesota Medicine*, 1940, **23**: 85.
2. BOYD, W.: Text Book of Pathology, Lea & Febiger, Phila., 3rd ed., 1938, p. 722.
3. DRESSER, R., MEIGS, J. V. AND RUDE, J. C.: Combined roentgen and radium treatment of carcinoma of the cervix, *Am. J. Roent. & Radium Therapy*, 1940, **43**: 17.
4. HARE, H. F.: The management of carcinoma of the cervix uteri, *Surg. Clin. of N. Am.*, **19**: (Lahey Clinic No.), 811.
5. HEALY, W. P.: Discussion on carcinoma of the cervix, *Am. J. Roent. & Radium Therapy*, 1940, **43**: 23.
6. MALIPHANT, R. G.: Complications in radiation treatment of carcinoma of the cervix, *J. Obst. & Gyn. Brit. Emp.*, 1939, **46**: 874.
7. MEIGS, J. V. AND JAFFE, H. L.: Carcinoma of the cervix treated by roentgen rays and radium, *Surg., Gyn. & Obst.*, 1939, **69**: 257.
8. MERRITT, E. A.: Roentgen therapy in cancer of the buccal cavity and of the cervix uteri, *Am. J. Roent. & Radium Therapy*, 1939, **42**: 418.
9. MOONEY, B. R.: Carcinoma of the breast: Some observations on preoperative treatment, *Canad. M. Ass. J.*, 1940 **43**: 580.
10. MORRISON, M. C.: Distribution of radiation in pervaginal roentgen therapy, *Radiol.*, 1940, **34**: 451.
11. PACK, G. T. AND LIVINGSTONE, E. M.: Treatment of Cancer and Allied Diseases, P. B. Hoeber, N.Y., 1940, **2**: 1606.
12. *Idem*: 1940, **2**: 1587.
13. *Idem*: 1940, **2**: 1588.
14. WALKER, J. Z.: Principles of radiation therapy in carcinoma of the cervix uteri, *Trans. Edinburgh Obst. Soc.*, 1938, **39**: 153. (In *Edinburgh M. J.*, Oct., 1939, **46**.)
15. WARREN, S., MEIGS, J. V., SEVERANCE, A. D. AND JAFFE, H. L.: The significance of radiation reaction in carcinoma of the cervix uteri, *Surg., Gyn. & Obst.*, 1939, **69**: 645.
16. WIRTH, J. E.: Carcinoma of the urinary bladder, cervix uteri and prostate treated by supravoltage roentgen rays, *Am. J. Roent. & Rad. Therapy*, 1938, **40**: 715.